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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/026,753	12/19/2001	Jayarama K. Shetty	GC695	2084

7590 09/22/2004

Genencor International, Inc.
925 Page Mill Road
Palo Alto, CA 94034-1013

EXAMINER

PRATS, FRANCISCO CHANDLER

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/026,753

Applicant(s)

SHETTY ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-18,21-34 and 37-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-18,21-34 and 37-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The amendment filed July 20, 2004, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 1, 2, 6-18, 21-34 and 37-51 are pending and are examined on the merits.

Claim Rejections - 35 USC § 102/103

Claims 46-51 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Antrim et al (U.S. Pat. 5,322,778).

The reference discloses a liquefied starch product which appears to be identical to the presently claimed product, based on the fact that the prior art product is a starch liquefact having a DE of 10.05, which is within the range recited in the claims, and a pH of 4.50, within the range recited in the claims, and being produced by an enzyme having essentially the same hydrolytic properties as the enzyme recited in the claims. See, column 7, lines 1-42. It is noted that the claims require the DE of about 10-12 to be reached within 60-75 minutes of adding the amylase. However, the fact remains that the claims recite a product made by contacting the same starting material as the prior art, under the same conditions as in the prior art,

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with the same enzyme as the prior art. Consequently, even if the process results in the desired product more quickly, the claimed liquefied starch product still appears to be anticipated by the reference.

It is noted that the enzyme used to produce the claimed product is from a different species of microorganism than the prior art enzyme. However, even if this results in a nominal difference between the reference product and the claimed product such that there is, in fact, no anticipation, the reference product would, nevertheless, have rendered the claimed product obvious to one of ordinary skill in the art at the time the claimed invention was made in view of the fact that one of ordinary skill would have expected nominal differences between starch liquefact products based on normal process variations between different hydrolysis batches and differences in enzyme batches. Thus the claimed invention as a whole was clearly *prima facie* obvious especially in the absence of sufficient, clear, and convincing evidence to the contrary.

Regarding the propriety of this type of alternative rejection, note that MPEP § 2113 states that:

. . . [w]hen the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is

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eminently fair and acceptable. As a practical matter, the Patent and Trademark Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith. *In re Brown*, 59 CCPA 1063, 173 USPQ 685 (1972).

MPEP § 2113 also clearly states that

'The Patent Office bears a lesser burden of proof in making out a case of *prima facie* obviousness for product-by-process claims because of their peculiar nature' than when a product is claimed in the conventional fashion. *In re Fessmann*, 180 USPQ 324 (CCPA 1974)."

Claim Rejections - 35 USC § 103

Claims 1, 2, 6-18, 21-34 and 37-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shetty et al ("Factors Affecting the Economics of Glucose Production," Delivering Innovation Through Biotechnology, Genencor International, Inc., (1998)) in view of JP 10-136979.

Shetty discloses a process of preparing glucose from starch, said process using the claimed process parameters. See, e.g. pages 6 and 14. Note in particular the disclosure on page 6 of the desirability of a liquefact having a DE of 10 to 12. Shetty differs from the claims in that Shetty uses a different α -amylase enzyme than that recited in the claims. However, Shetty discloses that α -amylases active at acidic pH are advantageous in processes of producing glucose from starch.

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Specifically, the liquefaction step is improved by decreasing chemical demand for pH adjustment, reducing color and by-product formation, and lowering refining requirements and costs (Shetty, page 7). Also, the lower pH afforded by the use of acidophilic α -amylase eliminates the undesirable formation of maltulose (Shetty, page 8). Shetty also discloses that enzymes which do not require calcium or stability are advantageous, as are relatively thermostable enzymes. Shetty, page 11, last sentence. ("It is evident from the above data that an improved thermostable alpha-amylase which can operate at a pH below 6.0 and at lower or no calcium will significantly reduce refining costs and improve the final glucose yield.")

As is evident from the English translation supplied herewith, JP '979 discloses an α -amylase which meets exactly the criteria disclosed by Shetty as being desirable and advantageous for use in the disclosed process of preparing glucose from starch. Specifically, the enzyme is thermostable, acid-stable, optimally active at a pH of about 4, and does not require calcium for activity (see Table 2). Thus, the artisan of ordinary skill practicing Shetty's process clearly would have recognized that the enzyme disclosed by JP '979 possesses all the properties required for use in Shetty's process. The artisan of ordinary skill would therefore clearly have been

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motivated to have used the enzyme of JP '979 in Shetty's process. A holding of obviousness is therefore required.

Because it is not clear that the enzyme units used in JP '979 correspond to the units used in applicant's claims, it is not clear that either reference discloses the use of the claimed amount of amylase. However, the artisan of ordinary skill at the time of applicant's invention clearly would have recognized that the rate of the liquefaction would have been readily optimized, depending on the amount of enzyme used. Thus, the claimed amounts of enzyme must be considered obvious in view of the fact that enzyme concentration was known to be a result-effective parameter, and therefore routinely optimized by artisan of ordinary at the time of applicant's invention.

Lastly, it is again noted that the claims require the DE of about 10-12 to be reached within 60-75 minutes of adding the amylase. However, it is respectfully submitted that this limitation does not serve to distinguish the claims from the cited prior art. Specifically, it is noted that at 75 minutes the DE of the various liquefaction processes disclosed by Shetty is about 9, which is encompassed by the lower limit of the presently claimed DE range of "about 10-12." See page 14 of Shetty, especially figs. 2 and 3. Moreover, the speed of an enzymatic reaction can be increased simply by increasing the

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ratio of enzyme to substrate, that is, by increasing the amount of enzyme or decreasing the amount of substrate. Thus, viewing the cited prior art, it is respectfully submitted that the artisan of ordinary skill had a reasonable expectation that the claimed DE could be reached in the claimed amount of time by following the teachings of Shetty and JP '979. A holding of obviousness is therefore required.

Response to Arguments

All of applicant's argument submitted to date, including that submitted July 20, 2004, has been fully considered but is not persuasive of error. While the Shetty publication does not disclose a liquefact having the both claimed DE and pH, it is respectfully submitted that it suggests such a product, as discussed herein, particularly when combined with JP '979. Moreover, as discussed above, it is respectfully submitted that the product-by-process claims encompass any amylase-liquefied starch having the claimed combination of DE (10 to 12) and pH (4.0 to 4.5), such as the product described by Antrim et al.

With respect to the obviousness rejection, it is respectfully submitted that the process parameters recited in applicant's claims are exactly those suggested by the Shetty references as being desirable, as well as being the process

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parameters disclosed by JP '979 as being the operating parameters of the *B. acidocaldarius* amylase. Thus, Shetty discloses the desirability of using a liquefying enzyme having a hydrolytic activity at a pH of 4.0 to 4.5, i.e. saccharification pH, which does not need a calcium cofactor, and JP '979 supplies exactly such an enzyme.

With respect to the assertion of unexpected results, it is respectfully pointed out that the velocity of any enzyme reaction depends on the concentration of both substrate and enzyme. See, for example, page 14 of Shetty, which specifies both enzyme and substrate amount when measuring the time of reaction. None of applicant's claims recites both of these parameters. Thus, simply reciting a length of time to achieve a specific DE does not demonstrate an unexpected result, since the speed of an enzymatic reaction can be increased simply by increasing the ratio of enzyme to substrate. Further still, in view of the fact that the kinetic abilities of the *B. acidocaldarius* amylase were known in the prior art by virtue of the disclosure of JP '979, it is not clear that applicant has demonstrated that the *B. acidocaldarius* amylase behaves in any way unexpectedly in view of the cited prior art.

The disclosed stability, or alleged lack thereof, of the enzyme of JP '979, pointed out by applicant, is noted. However,

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it is respectfully pointed out that the experimentally determined stabilities of enzymes seldom constrain the use of the enzymes in practical or commercial applications. For example, Example 3 of JP '979 (page 25 of translation submitted herewith), which exemplifies the use of the *B. acidocaldarius* enzyme in starch liquefaction, clearly discloses that the enzyme was subjected to heating to 90°C for 10 minutes, followed by heating to 130°C for 10 minutes, and then cooled to 90°C and maintained at that temperature for 60 minutes. Thus, JP '979 clearly contemplates using the claimed enzyme at the claimed temperatures for the claimed liquefaction durations. With respect to claim 44, it is respectfully pointed out that it appears that the high temperature cooking step is performed before the enzyme and starch are mixed. Either way, the 130°C for 10 minutes disclosed by JP '979 clearly provides a reasonable expectation that the enzyme would be useful under all of the conditions recited in applicant's claims. The obviousness rejection must therefore be maintained.

No claims are allowed.

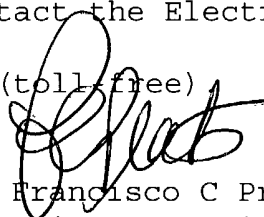
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco

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C Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Francisco C Prats
Primary Examiner
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FCP